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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/729,837	12/04/2003	Manne Satyanarayana Reddy	BULK 3.0-033	8513

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EXAMINER	
COPPINS, JANET L	
ART UNIT	**PAPER NUMBER**
1626	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/729,837	REDDY ET AL.	
	Examiner	Art Unit	
	Janet L. Coppins	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9 and 13-56* is/are pending in the application.

4a) Of the above claim(s) *17-32 and 35-56* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,13-16,33 and 34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-9 and 13-56 are currently pending in the instant application.

Response to Amendment

2. Receipt is acknowledged of Applicants' Amendment and Response, filed March 12, 2007, which has been reviewed by the Examiner and entered of record in the file. Accordingly, claims 10-12 have been cancelled, claim 16 has been amended, and claims 17-32 and 35-56 remain withdrawn from consideration.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 2 and 6-12 previously rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 10-12 have been cancelled, rendering the rejections moot.

(a) Claim 2 is rejected for incorporating a figure by reference. Applicants traverse the rejection, citing MPEP 2173.05(s) and arguing that the X-RDP for amorphous ziprasidone HCl cannot adequately be described, despite the Examiner's suggestions, and that the reference to Figure 1 is a more concise manner in which to claim the invention. Applicants also argue that incorporation by reference of X-RDP into patent claims is standard practice, citing several U.S. patents, including U.S. 6,852,747, also assigned to Examiner McKane. The Examiner respectfully disagrees, since the diffractometer provides the exact values for each peak based on a 2θ scale, and said values should be easily attainable by Applicants. Furthermore, Applicants

have neglected to label the y-axis of Figure 1 such that it is unclear what the 2θ values are measured against, e.g. intensity in counts per second.

The Examiner also directs Applicants' attention to *In re Geolette and Hoffman, 188 USPQ,* i.e. the Examiner is responsible for each case by himself, regardless of the actions of other Examiners. Regarding the '747 patent, the Examiner notes that not only are there no X-ray diffraction patterns present in the case, but claim 2 does not specifically refer to any pattern or figure by reference.

The Examiner maintains the rejection to claim 2 and recommends using language similar to the following, "The compound of claim 1, characterized by having significant X-ray powder diffraction pattern peaks expressed in 2θ values at ..."

(b) Claims 6-9 previously rejected for reciting, "...at least," which is indefinite, since the Specification lacks a standard for measuring the degree intended, i.e. there is no upper limit defined in the claims. Applicants traverse the rejection, arguing that the phrase, "at least" provides for greater amounts than the recited minimum amounts, up to 100%. The Examiner acknowledges that said compositions are inclusive of any composition that contains more than the recited minimum amount, and instead directs Applicants' attention to the obviousness rejections below.

10. Claim 16 previously rejected under 35 U.S.C. 112, first paragraph, as not being fully enabled. The Examiner notes with appreciation the amendatory changes to the claim, in which Applicants incorporate a specific disease known to be treated by ziprasidone, i.e. schizophrenia.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

13. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

14. Claims 1, 3-9, 13-16, 33 and 34 rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Pat. No. 4,831,031 to Lowe, III et al, in view of U.S. Pat. No. 6,150,366 to Arenson et al, further in view of Lieberman, "Pharmaceutical Dosage Forms."

Applicants are claiming the following compounds:

Applicants are claiming an amorphous form of ziprasidone hydrochloride.

Determining the scope and content of the prior art

The '031 patent teaches benzothiazole-piperazinyl-indole compounds and their hydrochloride salts, that have an identical structure to Applicants' ziprasidone hydrochloride, please refer to compounds according to Example 16 of columns 12-13, and specifically to the fourth compound of column 13, "5-(2-(4-(1,2-benzothiazol-3-yl)piperazinyl)ethyl-6-chlorooxindole hydrochloride."

The compounds disclosed in the '031 patent fully encompass the compounds of the instant invention and are known to have neuroleptic activity for treating psychotic disorders, including schizophrenia.

Ascertaining the difference between the prior art and the claims

The difference between the prior art and the claims is that the '031 patent does not teach a single disclosed amorphous form of ziprasidone hydrochloride that anticipates the instant claims.

Resolving the level of ordinary skill in the pertinent art

However, minus a showing of unobvious results, it would have been obvious to one of skill in the art to prepare the amorphous form of ziprasidone hydrochloride as instantly claimed in claim 1 since the prior art reference discloses the hydrochloride salt of ziprasidone. One would be motivated to prepare the instantly claimed invention since the '366 patent discusses ziprasidone compounds and pharmaceutical formulations and specifically teaches in column 1, lines 28-33,

> "[Ziprasidone] is typically administered as the hydrochloride acid addition salt. The hydrochloride salt is advantageous in that it is a high permeability drug, a factor which

> favorable affects bioavailability. The hydrochloride salt does, however, possess relatively poor aqueous solubility, a factor which unfavorably affects bioavailability. Low solubility compounds can be problematic in the pharmaceutical arts from a formulations perspective. Typical approaches can involve... formulating the drug in a small particle saize, therby increasing the surface area of the drug to facilitate more rapid dissolution."

Furthermore, referring to "Pharmaceutical Dosage Forms: Tablets" under "Bioavailability in Tablet Technology: Polymorphism" the authors state on pages 463-465 that,

> "Theoretical considerations predict that amorphous solids will, in general, be better absorbed than will crystalline ones. These considerations are based on the relative energies involved in the dissolution phenomena. An amorphous solid lacks strong cohesive bonds between the molecules. The molecules are randomly arranged, and less energy is required to separate the molecules of the amorphous material and dissolve the solid in contrast to the crystalline material. Techniques commonly used in preparing drugs in the amorphous state generally reduce the particle size of the drug and result in a faster rate of dissolution than occurs with a crystalline form."

Therefore, one skilled in the art would be motivated to make and use the amorphous form of the hydrochloride salt of ziprasidone (as taught by the '031 patent) and its pharmaceutical composition, known to be a useful antipsychotic for treating schizophrenia, in view of the '366 patent wherein the poor solubility of ziprasidone HCl is specifically discussed, guided by the Lieberman et al teaching of the advantages of amorphous forms, particularly when the amorphous from possesses the same activity and shares the same utility of treating psychotic disorders, with better bioavailability and improved solubility. Regarding the moisture content of claims 3-5, it would be known to one skilled in the art that amorphous forms of salts are typically prepared by spray-drying and therefore have a low moisture content, such that the recited percentages of 0.5%- 4.5% are inherent properties of an amorphous form of ziprasidone hydrochloride. Regarding claims 6-9, compositions containing ziprasidone hydrochloride are known (please refer to the '031 and '366 patents) and "at least" refers to anything greater than the minimum amount recited (e.g. 100% amorphous) and the Examiner has shown motivation for

preparing compositions containing amorphous ziprasidone hydrochloride, thus one skilled in the art would also have motivation for preparing the recited compositions.

Claims 33 and 34 are product-by-process claims, directed to an amorphous form of ziprasidone hydrochloride. Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985). Also see M.P.E.P. 2113.

Therefore, absent a showing of unobvious and superior properties, the instant claimed amorphous form of ziprasidone hydrochloride, its pharmaceutical composition, and method of use would have been suggested to one skilled in the art.

Conclusion

15. Claims 1-9 and 13-56 are pending in the application. Claims 17-32 and 35-56 are currently withdrawn, claims 1-9, 13-16, 33 and 34 are currently rejected, and.

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Coppins whose telephone number is 571.272.0680. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph K. McKane can be reached on 571.272.0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Janet L. Coppins
May 25, 2007

Joseph K. McKane
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SPE, Art Unit 1626